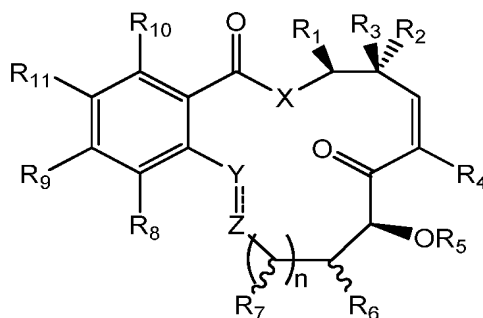


**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listing of claims in the application.

***Listing of Claims***

1. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R<sub>1</sub> is hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl;

R<sub>2</sub> is ~~C<sub>1-6</sub>-alkyl~~ methyl;

R<sub>3</sub> is hydrogen, ~~or halogen, hydroxyl, protected hydroxyl, or a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl moiety~~; or

~~R<sub>1</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;~~

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or an oxygen protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

~~R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~  
 R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy, ~~or a C<sub>1</sub>-C<sub>20</sub> alkyl,~~  
~~C<sub>2</sub>-C<sub>20</sub> alkenyl or C<sub>2</sub>-C<sub>20</sub> alkynyl moiety optionally substituted with hydroxyl, protected~~  
~~hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;~~  
 R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>,  
~~-X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected~~  
 hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl; or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety[[,]] ;

p is 2-10, and

R<sub>14</sub> is hydrogen, or a C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, C<sub>1</sub>-C<sub>20</sub> alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or C<sub>1</sub>-C<sub>20</sub> alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl moiety, or is -(C=O)NHR<sub>15</sub>, -(C=O)OR<sub>15</sub>, or -(C=O)R<sub>15</sub>, wherein each occurrence of R<sub>15</sub> is independently hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl; or R<sub>14</sub> is -SO<sub>2</sub>(R<sub>16</sub>), wherein R<sub>16</sub> is a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl or C<sub>2</sub>-C<sub>20</sub> alkynyl moiety, wherein one or more of R<sub>14</sub>, R<sub>15</sub>, or R<sub>16</sub> are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R<sub>8</sub> and R<sub>9</sub> may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with

hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R<sub>10</sub> is ~~hydrogen~~, hydroxyl, protected hydroxyl, or amino, ~~or protected amino~~;

R<sub>11</sub> is hydrogen, ~~hydroxyl or protected hydroxyl~~;

X is O;

Y is CHR<sub>17</sub>[[, C=O,]] or CR<sub>17</sub>; and Z is CHR<sub>18</sub>[[, C=O,]] or CR<sub>18</sub>[[,]] ;

wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is ~~independently~~ hydrogen, ~~C<sub>1</sub>-C<sub>20</sub>-alkyl, C<sub>2</sub>-C<sub>20</sub>-alkenyl or C<sub>2</sub>-C<sub>20</sub>-alkynyl~~ and wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

2. (currently amended) The composition of claim 1, wherein:

R<sub>1</sub> is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

~~R<sub>2</sub> is methyl;~~

R<sub>3</sub> is hydrogen, ~~halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub>-aryl,~~

~~wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or~~

~~R<sub>4</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;~~

~~R<sub>4</sub> is hydrogen or halogen;~~

~~R<sub>5</sub> is hydrogen or a protecting group;~~

~~R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;~~

~~n is 0-2;~~

~~R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~

~~R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;~~

~~R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>, -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;~~

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R<sub>14</sub> is hydrogen, or a C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl moiety, or is -(C=O)NHR<sub>15</sub>, -(C=O)OR<sub>15</sub>, or -(C=O)R<sub>15</sub>, wherein each occurrence of R<sub>15</sub> is independently hydrogen, alkyl, heteroalkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or R<sub>14</sub> is -SO<sub>2</sub>(R<sub>16</sub>), wherein R<sub>16</sub> is an alkyl moiety, wherein one or more of R<sub>14</sub>, R<sub>15</sub>, or R<sub>16</sub> are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

~~R<sub>8</sub> and R<sub>9</sub> may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with~~

~~hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; and~~

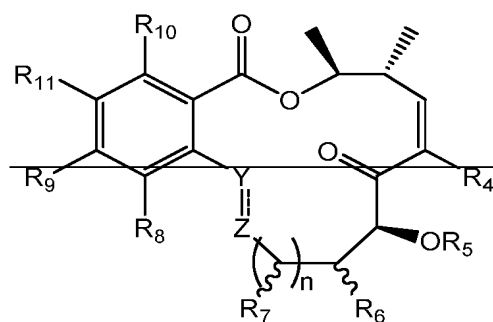
~~R<sub>10</sub> is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;~~

~~R<sub>11</sub> is hydrogen, hydroxyl or protected hydroxyl;~~

~~X is O;~~

~~Y is CHR<sub>17</sub>, C=O, or CR<sub>17</sub>; and Z is CHR<sub>18</sub>, C=O, or CR<sub>18</sub>, wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is independently hydrogen or lower alkyl, wherein Y and Z may be connected by a single or double bond.~~

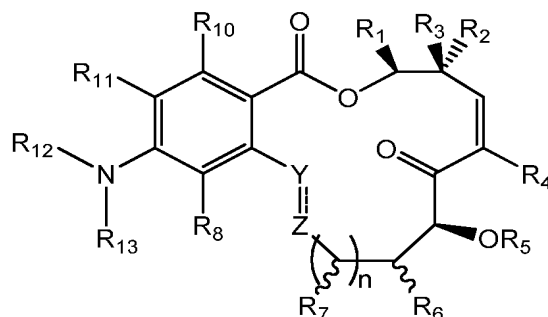
3. (currently amended) The composition of claim 2, where ~~and~~ n is 1.
4. (original) The composition of claim 2, where R<sub>4</sub> is halogen.
5. (original) The composition of claim 2, where R<sub>4</sub> is fluorine.
6. (original) The composition of claim 2, where Y and Z together represent -CH=CH-.
7. (original) The composition of claim 2, where Y and Z together represent trans -CH=CH-.
8. (currently amended) The composition of claim 2, wherein R<sub>1</sub> is ~~and R<sub>2</sub> are each~~ methyl ~~and R<sub>3</sub> is hydrogen and the compound has the structure:~~



~~wherein R<sub>4</sub>, R<sub>11</sub>, n, Y and Z are as defined in claim 2.~~

9. (previously presented) The composition of claim 8, wherein n is 1.
10. (original) The composition of claim 8, wherein R<sub>4</sub> is halogen.

11. (original) The composition of claim 8, wherein Y and Z together represent -CH=CH-.
12. (previously presented) The composition of claim 8, wherein n is 1, R<sub>4</sub> is halogen and Y and Z together represent -CH=CH-.
13. (original) The composition of claim 11 or 12 wherein -CH=CH- is trans.
14. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R<sub>1</sub> is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R<sub>2</sub> is C<sub>1-6</sub>-alkyl methyl;

R<sub>3</sub> is hydrogen[[,]] or halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R<sub>4</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R<sub>4</sub> is hydrogen or halogen;

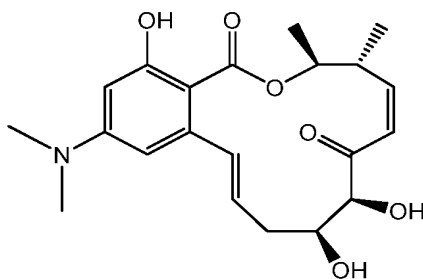
R<sub>5</sub> is hydrogen or [[a]] an oxygen protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

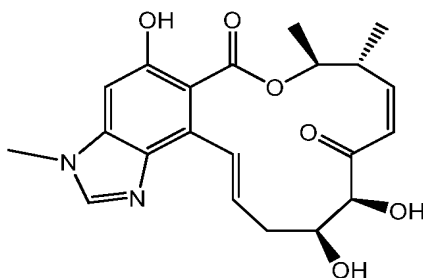
~~R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~  
R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy, ~~or lower alkyl~~  
~~optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;~~  
R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl,  
C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen  
protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated  
cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub>  
and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl,  
protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or  
halogen[[,]];  
R<sub>10</sub> is ~~hydrogen~~, hydroxyl, protected hydroxyl, or amino, ~~or protected amino~~;  
R<sub>11</sub> is hydrogen, ~~hydroxyl or protected hydroxyl~~;  
~~X is O;~~  
Y is CHR<sub>17</sub>[[, C=O,]] or CR<sub>17</sub>; and Z is CHR<sub>18</sub>[[, C=O,]] or CR<sub>18</sub>[[,]];  
wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is ~~independently~~ hydrogen ~~or lower alkyl~~,  
wherein Y and Z may be connected by a single or double bond, or  
R<sub>13</sub> and R<sub>8</sub> may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to  
3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino,  
alkylamino, aminoalkyl, and halogen;  
wherein oxygen protecting groups are selected from the group consisting of methyl  
ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-  
methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl  
ether, triethylsilylether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl  
ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate,  
dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting  
groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides,  
N-alkyl amines, N-aryl amines, imines, and enamines; and  
wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having  
from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one  
or two ring atoms are additional heteroatoms independently selected from S, O and N;  
and the remaining ring atoms are carbon.

15. (previously presented) The composition of claim 14, wherein n is 1.
16. (original) The composition of claim 14, wherein R<sub>4</sub> is halogen.
17. (original) The composition of claim 14, wherein Y and Z together represent -CH=CH-.
18. (currently amended) The composition of claim 14, wherein R<sub>1</sub> is and ~~R<sub>2</sub> are each~~ methyl and ~~R<sub>3</sub> is hydrogen~~.
19. (currently amended) The composition of claim 14, wherein n is 1, R<sub>1</sub> is and ~~R<sub>2</sub> are each~~ methyl, ~~R<sub>3</sub> is hydrogen~~, R<sub>4</sub> is halogen, and Y and Z together represent -CH=CH-.
20. (original) The composition of claim 17 or 19, wherein -CH=CH- is trans.
- 21-22. (canceled)
23. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

24. (previously presented) The composition of claim 14, wherein the compound has the structure:

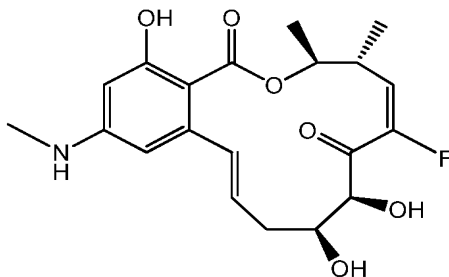




or a pharmaceutically acceptable salt or ester thereof.

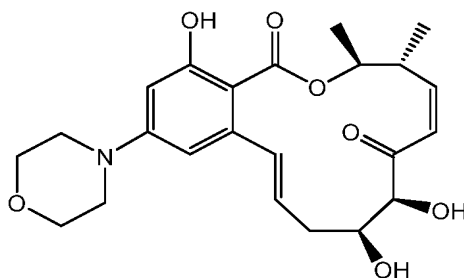
25-26. (canceled)

27. (previously presented) The composition of claim 14, wherein the compound has the structure:



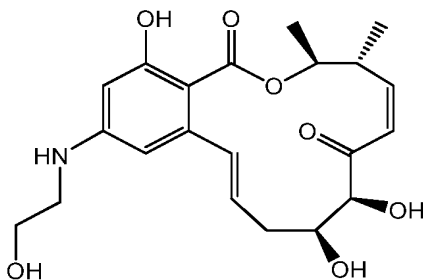
or a pharmaceutically acceptable salt or ester thereof.

28. (previously presented) The composition of claim 14, wherein the compound has the structure:



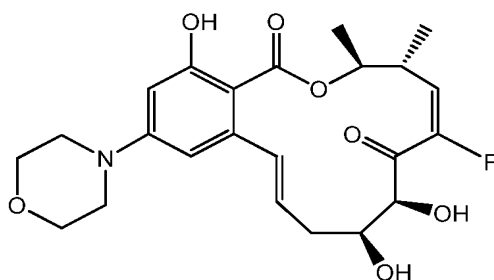
or a pharmaceutically acceptable salt or ester thereof.

29. (previously presented) The composition of claim 14, wherein the compound has the structure:



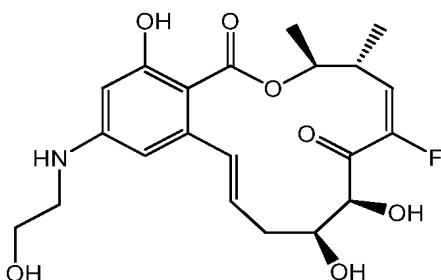
or a pharmaceutically acceptable salt or ester thereof.

30. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

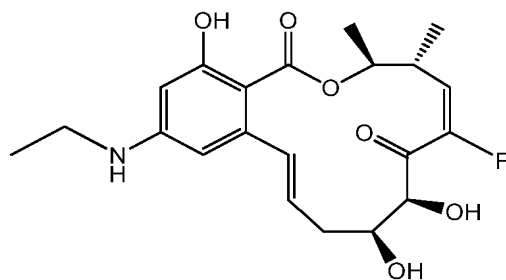
31. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

32. (canceled)

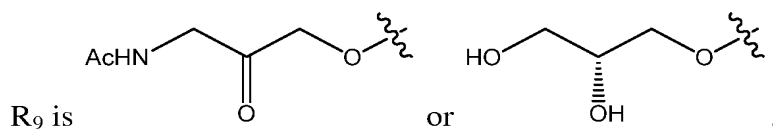
33. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

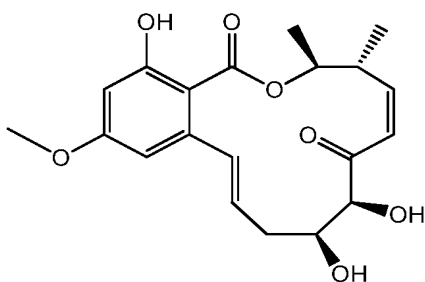
- 34-45. (canceled)

46. (withdrawn, currently amended) The composition of claim 2, where  $R_1$  is hydrogen ~~or methyl~~.
47. (withdrawn, currently amended) The composition of claim ~~[[2]]~~ 1, where  $R_3$  is ~~hydrogen or~~ halogen.
48. (withdrawn) The composition of claim 2, where  $R_4$  is hydrogen.
49. (withdrawn) The composition of claim 2, where  $R_5$  is hydrogen.
50. (withdrawn) The composition of claim 2, where  $R_6$  is hydroxyl.
51. (canceled)
52. (withdrawn, currently amended) The composition of claim ~~[[2]]~~ 1, where  $R_8$  is ~~hydrogen or~~ halogen.
53. (withdrawn) The composition of claim 2, where  $R_9$  is hydroxyl, protected hydroxyl,  $-OR_{12}$ ,  $-NR_{12}R_{13}$ , or  $-O(CH_2)_pX_2-R_{14}$ , wherein  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$  and  $X_2$  are as defined in claim 2.
54. (withdrawn, currently amended) The composition of claim 53, where  $R_9$  is  $-OR_{12}$ , wherein  $R_{12}$  is methyl, ethyl, propyl, isopropyl, butyl,  ~~$-CH_2COOMe$~~ , Bn, PMB (MPM), 3,4-ClBn, or



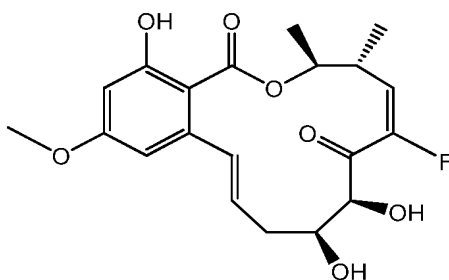
55.-61. (canceled)

62. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

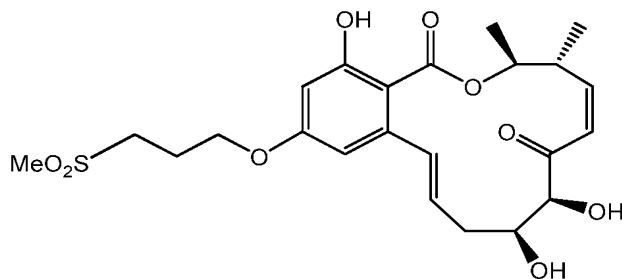
63. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

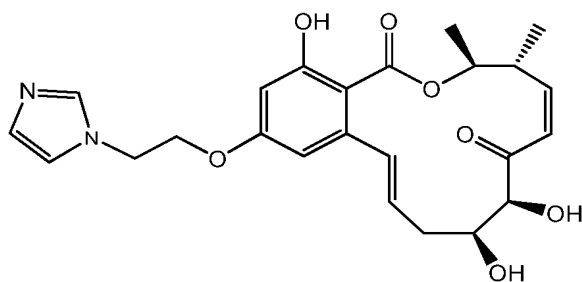
64. (canceled)

65. (previously presented) The composition of claim 1 wherein the compound has the structure:



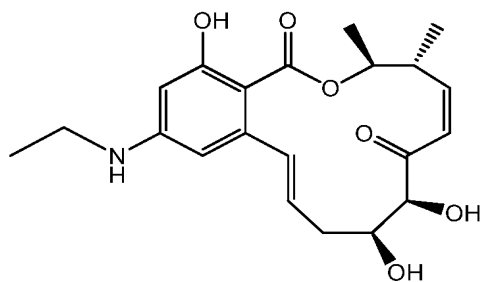
or a pharmaceutically acceptable salt or ester thereof.

66. (previously presented) The composition of claim 1 wherein the compound has the structure:



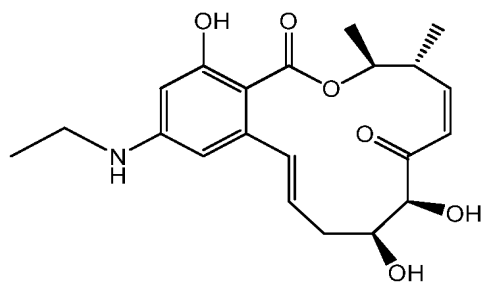
or a pharmaceutically acceptable salt or ester thereof.

67. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

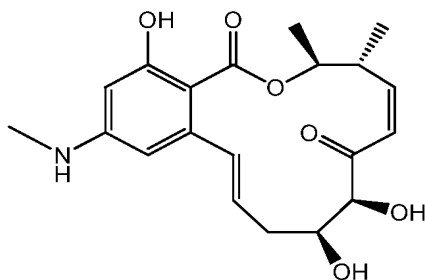


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

68. (new) The composition of claim 67, having the structure:

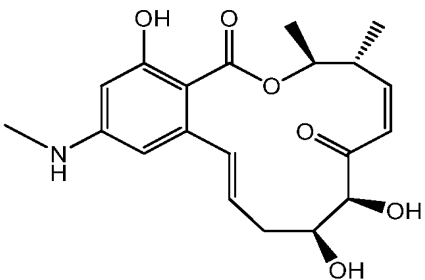


69. (new) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

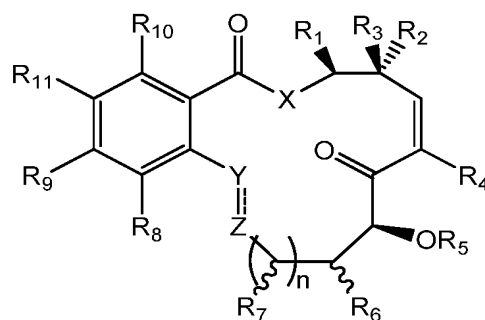


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

70. (new) The composition of claim 69, having the structure:



71. (new) The composition of claim 2, wherein  $R_4$ ,  $R_5$  and  $R_8$  are hydrogen,  $R_6$  and  $R_{10}$  are hydroxyl, and Y and Z together represent trans -CH=CH-.
72. (new) The composition of claim 71, wherein  $R_1$  is methyl.
73. (new) The composition of claim 14, wherein  $R_4$ ,  $R_5$  and  $R_8$  are hydrogen,  $R_6$  and  $R_{10}$  are hydroxyl, and Y and Z together represent trans -CH=CH-.
74. (new) The composition of claim 73, wherein  $R_1$  is methyl.
75. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

R<sub>1</sub> is hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl;

R<sub>2</sub> is methyl;

R<sub>3</sub> is hydrogen or halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or an oxygen protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub> is hydrogen;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy;

R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>,

-X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl; or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein  $X_1$  and  $X_2$  are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein  $X_2$ - $R_{14}$  together are  $N_3$  or are a saturated or unsaturated heterocyclic moiety;

p is 2-10, and

$R_{14}$  is hydrogen or a  $C_3$ - $C_{14}$  aryl,  $C_3$ - $C_{14}$  heteroaryl,  $C_1$ - $C_{20}$  alkyl( $C_3$ - $C_{14}$ )aryl, or  $C_1$ - $C_{20}$  alkyl( $C_3$ - $C_{14}$ )heteroaryl moiety, or is  $-(C=O)NHR_{15}$ ,  $-(C=O)OR_{15}$ , or  $-(C=O)R_{15}$ , wherein each occurrence of  $R_{15}$  is independently hydrogen,  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_1$ - $C_{20}$  heteroalkyl,  $C_2$ - $C_{20}$  heteroalkenyl,  $C_2$ - $C_{20}$  heteroalkynyl,  $C_3$ - $C_{20}$  cycloalkyl,  $C_3$ - $C_{20}$  cycloalkenyl,  $C_3$ - $C_{20}$  cycloalkynyl,  $C_3$ - $C_{20}$  heterocycloalkyl,  $C_3$ - $C_{20}$  heterocycloalkenyl,  $C_3$ - $C_{20}$  heterocycloalkynyl,  $C_3$ - $C_{14}$  aryl or  $C_3$ - $C_{14}$  heteroaryl; or  $R_{14}$  is  $-SO_2(R_{16})$ , wherein  $R_{16}$  is a  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl or  $C_2$ - $C_{20}$  alkynyl moiety, wherein one or more of  $R_{14}$ ,  $R_{15}$ , or  $R_{16}$  are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

$R_8$  and  $R_9$  may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$R_{10}$  is hydroxyl, protected hydroxyl, or amino;

$R_{11}$  is hydrogen;

X is O;

Y is  $CHR_{17}$  or  $CR_{17}$ ; and Z is  $CHR_{18}$  or  $CR_{18}$ ;

wherein each occurrence of  $R_{17}$  and  $R_{18}$  is hydrogen and wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyl dimethylsilyl ether, tribenzyl silyl ether, t-butyl diphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and



wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

76. (new) The composition of claim 75, wherein:

R<sub>1</sub> is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R<sub>3</sub> is hydrogen;

R<sub>8</sub> is hydrogen;

R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>,

-X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

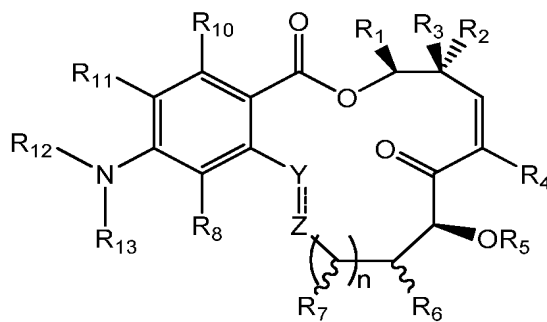
wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R<sub>14</sub> is hydrogen, or a C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl moiety, or is -(C=O)NHR<sub>15</sub>, -(C=O)OR<sub>15</sub>, or -(C=O)R<sub>15</sub>, wherein each occurrence of R<sub>15</sub> is independently hydrogen, alkyl, heteroalkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or R<sub>14</sub> is -SO<sub>2</sub>(R<sub>16</sub>), wherein R<sub>16</sub> is an alkyl moiety, wherein one or more of R<sub>14</sub>, R<sub>15</sub>, or R<sub>16</sub> are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; and

R<sub>10</sub> is hydroxyl.

77. (new) The composition of claim 76, where n is 1.
78. (new) The composition of claim 76, where R<sub>4</sub> is halogen.
79. (new) The composition of claim 76, where R<sub>4</sub> is fluorine.
80. (new) The composition of claim 76, where Y and Z together represent -CH=CH-.
81. (new) The composition of claim 76, where Y and Z together represent trans -CH=CH-.
82. (new) The composition of claim 76, wherein R<sub>1</sub> is methyl.
83. (new) The composition of claim 82, wherein n is 1.
84. (new) The composition of claim 82, wherein R<sub>4</sub> is halogen.
85. (new) The composition of claim 82, wherein Y and Z together represent -CH=CH-.
86. (new) The composition of claim 82, wherein n is 1, R<sub>4</sub> is halogen and Y and Z together represent -CH=CH-.
87. (new) The composition of claim 85 or 86 wherein -CH=CH- is trans.
88. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

R<sub>1</sub> is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R<sub>2</sub> is methyl;

R<sub>3</sub> is hydrogen or halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or an oxygen protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub> is hydrogen;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy;

R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R<sub>10</sub> is hydroxyl, protected hydroxyl, or amino;

R<sub>11</sub> is hydrogen;

Y is CHR<sub>17</sub> or CR<sub>17</sub>; and Z is CHR<sub>18</sub> or CR<sub>18</sub>;

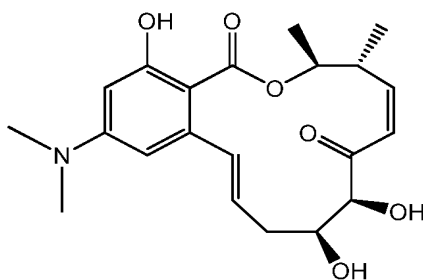
wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is hydrogen, wherein Y and Z may be connected by a single or double bond, or

R<sub>13</sub> and R<sub>8</sub> may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl

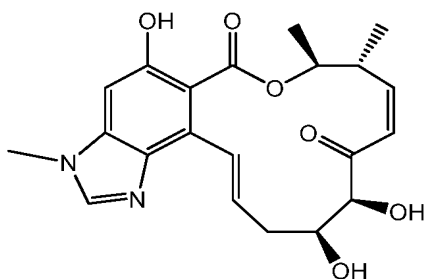
ether, t-butyl diphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

89. (new) The composition of claim 88, wherein n is 1.
90. (new) The composition of claim 88, wherein R<sub>4</sub> is halogen.
91. (new) The composition of claim 88, wherein Y and Z together represent -CH=CH-.
92. (new) The composition of claim 88, wherein R<sub>1</sub> is methyl.
93. (new) The composition of claim 88, wherein n is 1, R<sub>1</sub> is methyl, R<sub>4</sub> is halogen, and Y and Z together represent -CH=CH-.
94. (new) The composition of claim 91 or 93, wherein -CH=CH- is trans.
95. (new) The composition of claim 88, wherein the compound has the structure:



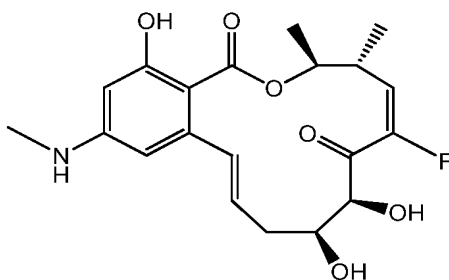
or a pharmaceutically acceptable salt or ester thereof.

96. (new) The composition of claim 88, wherein the compound has the structure:



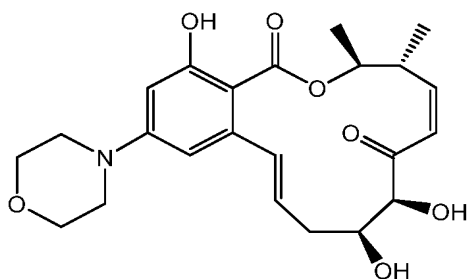
or a pharmaceutically acceptable salt or ester thereof.

97. (new) The composition of claim 88, wherein the compound has the structure:



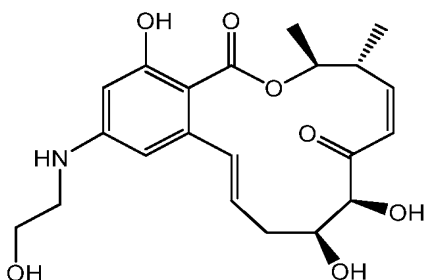
or a pharmaceutically acceptable salt or ester thereof.

98. (new) The composition of claim 88, wherein the compound has the structure:



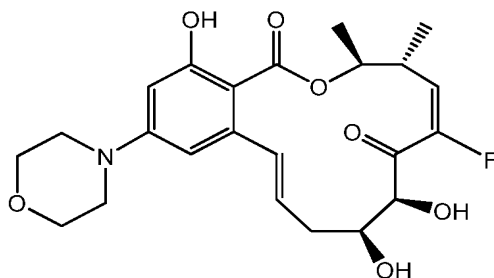
or a pharmaceutically acceptable salt or ester thereof.

99. (new) The composition of claim 88, wherein the compound has the structure:



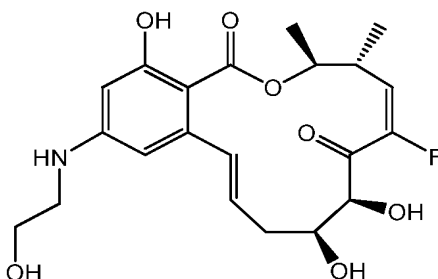
or a pharmaceutically acceptable salt or ester thereof.

100. (new) The composition of claim 88, wherein the compound has the structure:



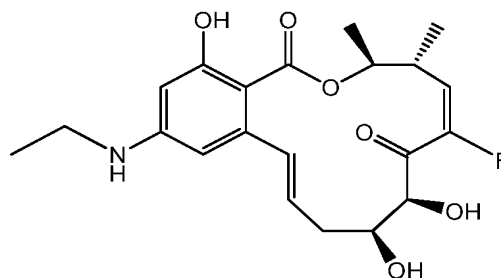
or a pharmaceutically acceptable salt or ester thereof.

101. (new) The composition of claim 88, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

102. (new) The composition of claim 88, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

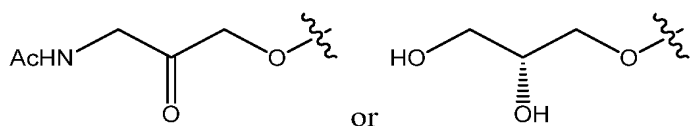
103. (new) The composition of claim 76, where R<sub>1</sub> is hydrogen.

104. (new) The composition of claim 75, where R<sub>3</sub> is halogen.

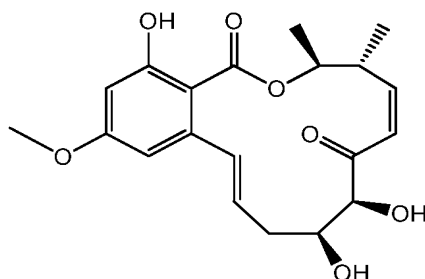
105. (new) The composition of claim 76, where R<sub>4</sub> is hydrogen.

106. (new) The composition of claim 76, where R<sub>5</sub> is hydrogen.

107. (new) The composition of claim 76, where  $R_6$  is hydroxyl.
108. (new) The composition of claim 75, where  $R_8$  is halogen.
109. (new) The composition of claim 76, where  $R_9$  is hydroxyl, protected hydroxyl,  $-OR_{12}$ ,  $-NR_{12}R_{13}$ , or  $-O(CH_2)_pX_2-R_{14}$ , wherein  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$  and  $X_2$  are as defined in claim 76.
110. (new) The composition of claim 109, where  $R_9$  is  $-OR_{12}$ , wherein  $R_{12}$  is methyl, ethyl, propyl, isopropyl, butyl, Bn, PMB (MPM), 3,4-ClBn, or  $R_9$  is

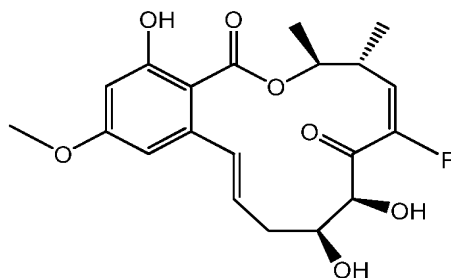


111. (new) The composition of claim 75 wherein the compound has the structure:



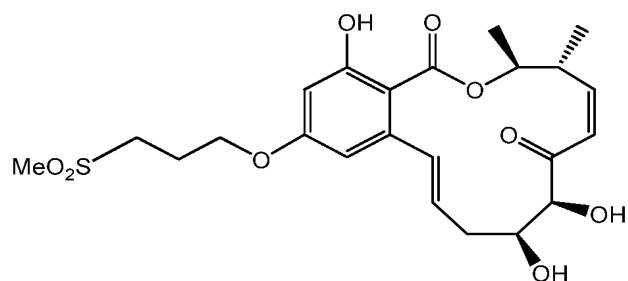
or a pharmaceutically acceptable salt or ester thereof.

112. (new) The composition of claim 75 wherein the compound has the structure:



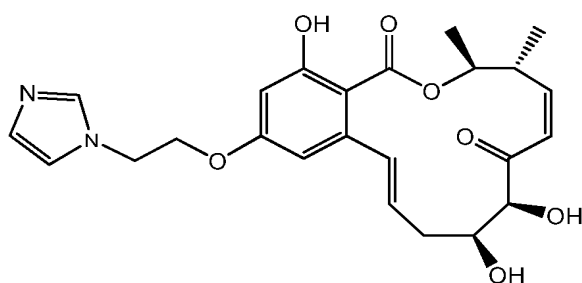
or a pharmaceutically acceptable salt or ester thereof.

113. (new) The composition of claim 75 wherein the compound has the structure:



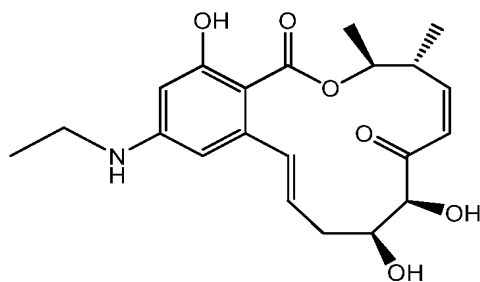
or a pharmaceutically acceptable salt or ester thereof.

114. (new) The composition of claim 75 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

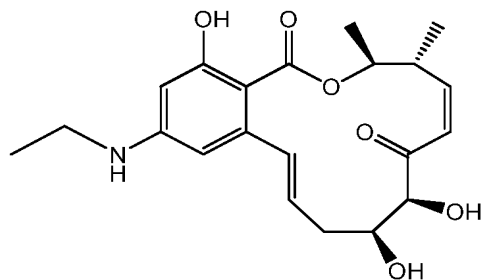
115. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



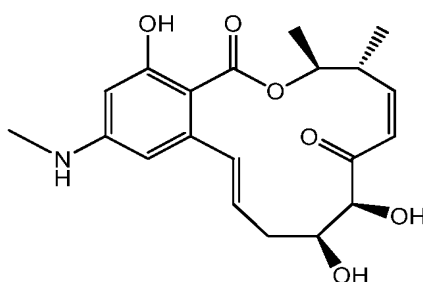
or a pharmaceutically acceptable salt, ester, or salt of ester thereof.



116. (new) The composition of claim 115, having the structure:

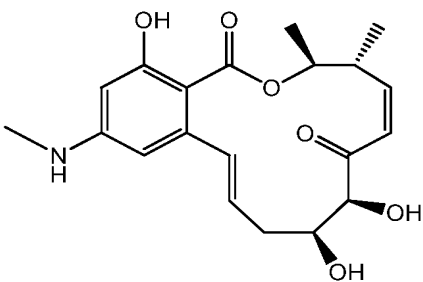


117. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

118. (new) The composition of claim 117, having the structure:



119. (new) The composition of claim 76, wherein  $R_4$ ,  $R_5$  and  $R_8$  are hydrogen,  $R_6$  and  $R_{10}$  are hydroxyl, and Y and Z together represent trans -CH=CH-.
120. (new) The composition of claim 119, wherein  $R_1$  is methyl.
121. (new) The composition of claim 88, wherein  $R_4$ ,  $R_5$  and  $R_8$  are hydrogen,  $R_6$  and  $R_{10}$  are hydroxyl, and Y and Z together represent trans -CH=CH-.
122. (new) The composition of claim 121, wherein  $R_1$  is methyl.